

AMENDMENT UNDER 37 C.F.R. § 1.111  
U.S. Application No.: 09/870,676

**REMARKS**

Upon entry of this amendment, claims 1, 5, 6, 9-15, and 17-20 are all the claims pending in the application.

Claims 2-4, 7, 8, and 16 are canceled.

Claim 1 is amended to incorporate the recitation of dependent claim 5. R<sup>1</sup> is amended to “... biphenyl or [and] naphthyl group.”

Claim 5 is amended by deleting the definitions of R<sup>3</sup> and R<sup>4</sup> and the recitation of claims 2 or 3.

Claim 9 is amended to correct a typographical error. “[F]ormula (2)” is changed to “formula (3),” in accordance with the Examiner’s statement.

Claim 12 has been amended to replace “the amine” by “the organic base.” Support is found in base claim 1. No new matter is added.

Claims 9-14 are amended to change dependency to include dependency on new claims 17-20.

New independent claim 17 is added, which is based on claims 5 and 15. No new matter is added.

New independent claim 18 is added, which is based on claims 1 and 6 with editorial changes to obviate the objection to original claim 6. No new matter is added.

New claim 19 is added, which is based on claims 1 and 7.

New claim 20 is added, which is a dependent claim from claim 19, and is based on original claims 7 and 8.

No new matter is added. It is respectfully requested that the amendment be entered.

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Claims 5, 6, 8, 9 and 12-15 are rejected under 35 U.S.C. §112, second paragraph, as indefinite. It is stated that the substituents  $R^3$  and  $R^4$  defined in claim 5 are not present in claim 1. Therefore, it is asserted that there is no antecedent basis for the substituents  $R^3$  and  $R^4$  in claim 5 as it depends from 1. It is further asserted that claim 5 is indefinite due to the word “and” being present between biphenyl and naphthyl. Claims 6 and 8 depend from claim 5, which has been found to be indefinite, therefore claims 6 and 8 are also rejected as indefinite.

In response, claim 5 is amended to omit  $R^3$  and  $R^4$ . The “and” between biphenyl and naphthyl has been deleted in favor of “or.”

It is asserted that claim 8 is indefinite because there is no antecedent basis for the carboxylic acid of formula (7). The only claim specifying a carboxylic acid of formula (7) is claim 7, which is not drawn to the elected invention. Thus, claim 8 has not been considered on the merits.

In response, claim 8 is canceled. Applicants reserve the right to prosecute the subject matter in canceled claim 8 in a divisional application.

It is asserted that, in claim 9, the phrase “said carboxylic acid activating agent of formula (2)” refers to claim 1. The carboxylic acid activating agent in claim 1 is designated formula (3). Thus, claim 9 has been examined on the merits as if it referred to the carboxylic acid activating agent as being defined by the formula (3).

In response, claim 9 has been amended to correct this typographical error.

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Claim 12 is rejected for reference to “the amine” in claim 1. It is stated that there is not antecedent basis for the amine referred to in claim 1. Therefore, claim 12 has been examined on the merits as if “the amine” were replaced by “the organic base.”

In response, claim 12 is amended accordingly.

Claims 13-15 are rejected for lack of antecedent basis. Each depends from claim 1 and recites the molar ratio (with respect to the carboxylic acid), the identity, and the order in which the organic base is added to other reagents. However, each of claims 13-15 refers to the organic base as “the base,” which is broader in scope than “organic base.” Thus, it is stated that there is not antecedent basis for any base other than an organic base in claim 1. It is suggested that claims 13-15 should be amended to refer to the “the organic base” in claim 1.

In response, the claims have been amended accordingly.

As amended, the claims are definite and patentable. For the reasons set forth above, it is respectfully requested that the rejections be reconsidered and withdrawn.

Claims 1, 5, and 11 are rejected under 35 U.S.C. §102(b) as anticipated by E. J. Bourne et al, Journal of the American Chemical Society, pages 2006-2012 (1954) (“Bourne”). Bourne is asserted to disclose the synthesis of trifluoroacetyl acetate from trifluoroacetic anhydride and acetic acid in equimolar amounts, catalyzed by pyridine.

It is stated that in order to make the trifluoroacetic anhydride and acetic acid solution of Bourne, acetic acid must have been added to trifluoroacetic anhydride. It is asserted that afterwards, an organic base (pyridine) was added to the resultant trifluoroacetic anhydride-containing solution.

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In response, the independent claims are amended to specify that the carboxylic acid and organic base must be added simultaneously to the solution of the carboxylic acid activating agent. Moreover, Bourne merely discloses at The Experimental on page 2008 a method of preparing a mixed anhydride of trifluoroacetic acid and acetic acid by adding pyridine to a mixture of trifluoroacetic anhydride and acetic acid. The reference does not teach a method of adding a carboxylic acid and a base to a carboxylic acid activating agent.

Therefore, it is respectfully requested that the rejection be reconsidered and withdrawn.

Claims 1, 5, 9-13 and 15 are rejected under 35 U.S.C. §102(b) as anticipated by Urbanski et al, Polish Journal of Chemistry, vol. 58, pages 1227-1229 (1984) ("Urbanski"). Urbanski is asserted to disclose the synthesis of mixed sulfonic-carboxylic anhydrides from benzenesulfonyl chloride and various aromatic carboxylic acids. The amounts of carboxylic acid, benzenesulfonyl chloride (the carboxylic acid activating agent) and organic base (either pyridine or triethylamine) are asserted to be equimolar (0.02 mole).

Applicants respectfully traverse. Urbanski discloses at page 1229 that benzenesulfonyl chloride was added to a mixture of a carboxylic acid and a tertiary amine in Stage 1. The carboxylic acid and a tertiary amine were not added to benzenesulfonyl chloride, as recited in the present claims.

In Stage 2, the carboxylic acid activating agent is an asymmetrical mixed acid anhydride, which is outside the scope of the carboxylic activating agent of formula (3) of the present invention.

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The asserted reference also notes that the order of addition did not have significant effect of the yield of the unsymmetrical anhydride at the last two lines of the paragraph of page 1228, which teaches away the presently claimed process. Applicants refer to the experimental results of Table 1 on page 28 and that of pages 44 and 45 of the present specification, showing the clear superiority of the claimed method of simultaneous addition.

Moreover, there is no disclosure or teaching of a process of a mixed acid anhydride using the carboxylic acid of formula (8).

Therefore, the amended claims are not anticipated by Urbanski. For at least these reasons, it is respectfully requested that the rejection be reconsidred and withdrawn.

Claims 1, 5, 11 and 15 are rejected under 35 U.S.C. § 102(b) as being anticipated by Gaede, B., Organic Process Research and Development, Vol. 3, pages 92-93 (1999). (“Gaede”).

It is asserted that diethyl chlorophosphate is the carboxylic acid activating agent employed in the Gaede reference. It is asserted that all of the limitations of claims 1, 5, 11 and 15 are disclosed in the section headed “Results” starting on page 92 to page 93 (including Table 1) and “General Procedure” on page 93.

In response, Applicants respectfully traverse. Gaede discloses in the Experimental Section at the right column on page 93, a method of adding diethylchlorophosphate to a mixture of a carboxylic acid and triethylamine in tetrahydrofuran solution, but does not teach the presently claimed method.

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As presently claimed, carboxylic acid and organic base must be added simultaneously to the solution of the carboxylic acid activating agent. Therefore, the amended claims are not anticipated by Gaede, and it is requested that the rejection be withdrawn.

Claims 1, 5, 9, 11 and 15 are rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent 4,874,558 ("Fife"). Fife is asserted to disclose polymeric 4-vinyl pyridine (P4-VP) catalyzed synthesis of mixed anhydrides from carboxylic acid chlorides and carboxylic acids. It is stated that Example 1 and Table 1 disclose all of the limitations of claims 1, 5, 11 and 15.

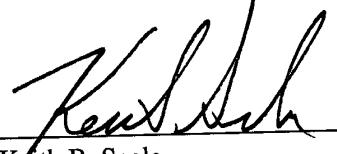
In response, Applicants respectfully traverse. Fife discloses a method of producing a mixed acid anhydride by reacting a mixture of an acid chloride, carboxylic acid, and P4-VP (a solid-phase copolymer 4-vinylpyridine) or a method of treating a mixture of carboxylic acid and P4-VP with thionyl chloride, but Fife does not teach the presently claimed process, for at least the reasons set forth above in response to the other rejections. Therefore, it is respectfully requested that the rejection be reconsidered and withdrawn.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

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The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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Date: February 19, 2003

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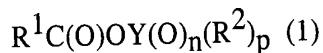
APPENDIX  
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

**Claims 2-4, 7, 8 and 16 are canceled.**

**The claims are amended as follows:**

1. (Amended) A method for producing a mixed acid anhydride of formula (1):



wherein  $R^1$ ,  $R^2$ , Y, n and p denote the same as defined below,

which comprises simultaneously adding

a carboxylic acid of formula (2);



wherein  $R^1$  denotes

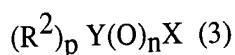
a hydrogen atom,

an optionally substituted alkyl group,

an optionally substituted aryl group, or

an optionally substituted hetero ring, and

an organic base to a solution of a carboxylic acid activating agent of formula (3);



wherein  $R^2$  denotes

an optionally substituted aliphatic hydrocarbyl group,

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an optionally substituted aromatic hydrocarbyl,  
an optionally substituted chain or cyclic alkoxy group, or  
an optionally substituted aryloxy group,

Y denotes

a carbon atom, a phosphorus atom, or a sulfur atom,

X denotes

a fluorine atom, a chlorine atom, a bromine atom, an iodine atom, a cyano group or a group of formula:

$(R^2)_p Y(O)_n O^-$ ,

wherein  $R^2$  is the same as defined above,

n and p are an integer of 1 or 2; and

when Y is a carbon atom, n=1 and p=1,

when Y is a phosphorous atom, n=1 and p=2, and

when Y is sulfur atom, n=2 and p=1 and  $R^2$  denotes an optionally substituted alkyl or aryl group.

5. (Amended) A method according to claim 1, [2 or 3], wherein  $R^1$  denotes a hydrogen atom, a straight, branched or cyclic (C1-C17)alkyl group, a (C2-C5)alkenyl or (C5-C6)cycloalkenyl group, a (C3-C4) alkynyl group, a phenyl, tolyl, biphenyl or [and] naphthyl group, an aralkyl, arylalkenyl or arylalkynyl group, a pyridyl group, a 1,3-oxazole group, a 1,3-thiazole group, a furyl group, a tetrahydrofuryl group, a thienyl group,

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an imidazole or (C2-C11)alkyleneimine group of which nitrogen atoms are protected by a protecting,

wherein said groups other than hydrogen atom may be substituted with

- (a) a hydroxy group or a halogen atom, or
- (b) an amino group of formula:

$R^{11}R^{12}N^-$  and

optionally further with at least one group selected from

a carbamoyl group, a methylmercapto group, a 4-pyrimidinone-3-yl group, an alkyl(C1-C3)dithio group, of which alkyl is substituted with a protected amino and carboxyl groups, a mercapto, guanidyl, carboxyl, hydroxy or imidazolyl group,

wherein

$R^{11}$  represents a hydrogen atom or an amino-protecting group,

$R^{12}$  represents an amino-protecting group, or a group of formula:  $R^{13}-CO$ ,

wherein  $R^{13}$  represents a saturated or unsaturated hydrocarbyl group or a hetero ring, which may be substituted with (c) a hydroxy group, or a halogen atom, or a group of formula:  $R^{14}R^{15}N^-$  and optionally further with at least one group selected from

a carbamoyl group, a methylmercapto group, an alkyl (C1-C3) dithio group, of which alkyl is substituted with an amino and carboxyl groups, an amino, mercapto, guanidyl, carboxyl, hydroxy, imidazolyl group,

wherein  $R^{14}$  is an amino-protecting group, and

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$R^{15}$  represents a hydrogen atom, a saturated or unsaturated hydrocarbyl group, a hetero ring or an amino-protecting group.

$R^3$  and  $R^4$  independently denote a chain, branched or cyclic (C1-C18)alkyl group, a (C2-C5)alkenyl or (C5-C6)cycloalkenyl group, a (C3-C4)alkynyl group, a phenyl, tolyl, biphenyl and naphthyl group, an aralkyl, arylalkenyl or arylalkynyl group, a hetero ring selected from a pyridyl group, a 1,3-oxazole group, a 1,3-thiazole group, a furyl group, a tetrahydrofuryl group, a thienyl group, an imidazole or a (C2-C11) alkyleneimine group of which nitrogen atoms are protected by a protecting group, all of which may be substituted with at least one group selected from a halogen, nitro, (C1-C3) alkoxy, (C1-C3) alkyl, hydroxy, cyano group, or (2-alkoxyiminoacetate)-2-yl group, a carbamoyl group, a methylmercapto group, an alkyl (C1-C3) dithio group, of which alkyl is substituted with a protected amine and carboxyl groups, an amino, mercapto, guanidyl, carboxyl, hydroxy, imidazolyl group, a group of formula:  $C(O)R^8$ , wherein  $R^9$  is an alkoxy group or a group of formula:  $NHR^{20}$  wherein  $R^8$  and  $R^2$  represents a saturated or unsaturated hydrocarbyl group or the hetero ring, both of which may be substituted with a group of formula:  $C(O)R^{81}$  or a hydroxy group and optionally further with at least one group selected from a carbamoyl group, a methylmercapto group, alkyl (C1-C3) dithio group, of which alkyl is substituted with an amino and carboxyl groups, an amino, mercapto, guanidyl, carbomyl, hydroxy, or imidazolyl group, wherein  $R^{81}$  is an alkoxy group or a group of formula:  $NHR^{92}$  wherein  $R^{81}$  and  $R^{82}$  represent a saturated or unsaturated hydrocarbyl group or a

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hetero ring, R<sup>3</sup> may represent a group of formula: -OR<sup>20</sup>, or NR<sup>30</sup>R<sup>31</sup>, wherein R<sup>30</sup> represents an optionally substituted alkyl group, or an optionally substituted aryl group and R<sup>31</sup> represents a hydrogen atom or an optionally substituted aryl group, and R<sup>3</sup> and R<sup>40</sup> may represent a hydrogen atom, or a protective group for an amine group,] provided that said amino, mercapto, guanidyl, carboxyl, hydroxy and imidazolyl groups which may be present in R<sup>1</sup>, R<sup>2</sup>, [R<sup>3</sup>] and substituent groups contained therein are in a protected form,[R<sup>3</sup> and R<sup>4</sup> may be bonded to form a ring,]  
R<sup>2</sup> denotes a chain, branched or cyclic (C1-C6) alkyl group, which may be substituted with a halogen atom, a phenyl which may be substituted with a halogen or (C1-C3) alkyl group, a chain or cyclic (C1-C6) alkoxy group, or a phenoxy group which may be substituted with a halogen or C1-C3 alkyl group.

6. (Amended) A method according to claim 5, wherein R<sup>1</sup> represents a group of formula (6): R<sup>11</sup>R<sup>12</sup>N-A- (6)  
wherein R<sup>11</sup> and R<sup>12</sup> are [the same] as defined in claim 5, and [“A”] represents an alkylene group, an alkenylene group, an alkynylene group, an arylene group, an aralkylene group, an arylalkenylene group, an arylalkynylene group, an oxazole ring, a thiazole ring, or an imidazole ring.

9. (Amended) The method according to [any one of claims] claim 1, 17, 18, 19 or 20 [to 3], wherein said carboxylic acid activating agent [defined by said formula (2)] of formula (3) is an acid chloride [(X-Cl)].

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10. (Amended) The method according to [any one of claims] claim 1, 17, 18, 19, or 20 [to 3], wherein the amount of the organic base is 0.9 to 2 moles per mol of said carboxylic acid in the production of the mixed acid anhydride [defined by said general] of formula [(3)] (1).

11. (Amended) The method according to [claims] claim 1, 17, 18, 19, or 20 [or 2,] wherein the amount of the carboxylic acid activating agent is 0.95 to 1.05 moles per mol of the carboxylic acid of formula (2).

12. (Amended) The method according to claim 1, 17, 18, 19, or 20 [or 2], wherein the amount of the organic base [amine] is 0.95 to 1.05 mol per mol of the carboxylic acid of formula (2).

13. (Amended) The method according to claim 1, 17, 18, 19, or 20, wherein the amount of the organic base per mol of the carboxylic acid of formula (2) is substantially equimolar.

14. (Amended) The method according to claim 1 [or 2,] 17, 18, 19, or 20, wherein the organic base is N-methylmorpholine.

15. (Amended) The method according to claim [1] 18, 19, or 20, wherein the base and the carboxylic acid are simultaneously added.

**Claims 17-20 are added as new claims.**